THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY,

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DISSERTATION ON

" THE PREVALENCE OF URINARY TRACT INFECTIONS IN PATIENTS WITH CHRONIC KIDNEY DISEASE "

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BRANCH – I

(GENERAL MEDICINE)

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CERTIFICATE

This is to certify that the Dissertation entitled **"THE PREVALENCE OF URINARY TRACT INFECTIONS IN PATIENTS WITH CHRONIC KIDNEY DISEASE"** is a bonafide record of work done by **Dr.V.RAVICHANDRAN** in the department of Medicine, Thanjavur Medical College, Thanjavur, during his Post Graduate Course from 2008 to 2011. This is submitted as partial fulfillment for the requirement of **M.D.,** Degree examinations – Branch –I (General Medicine) to be held in April 2011.

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I, **Dr. V.RAVICHANDRAN**, solemnly declare that the dissertation titled **"THE PREVALENCE OF URINARY TRACT INFECTIONS IN PATIENTS WITH CHRONIC KIDNEY DISEASE"** is a bonafide work done by me at Thanjavur Medical College Hospital, Thanjavur, during Dec 2009 – Nov 2010.

The dissertation is submitted to **"The Tamilnadu Dr. M.G.R. Medical University, Chennai",** Tamilnadu as a partial fulfillment for the requirement of **M.D** Degree examinations – Branch –I (General Medicine) to be held in April 2011.

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CONTENTS

INTRODUCTION

Urinary tract infection is the most common of all bacterial infections affecting humans through out their life span. The estimated incidence of urinary tract infection in developed countries is as high as 8 -10 million per year. 36.3% in hospitalised patients and 16.5% in non-hospitalised patients. Urinary tract infections are the leading cause A gram negative sepsis in hospitalised patients[1].

The incidence of urinary tract infection is influenced by age, sex and by predisposing factors that impair the defence mechanisms that maintain the sterility of urinary tract.

In chronic kidney disease dysfunction of the host defences is one of the major functional disturbances and result in increased susceptibility to various infections[2]. Besides urosepsis and septicemia they result in further deterioration of metabolic profile in these patients. Although potentially curable, the diagnosis is often difficult as many of the distinguishing features of infection may be absent in renal failure. The functional impairment of polymorphonuclear cells, impairment of cell mediated and humoral immunity, malnutrition and dialysis procedure may contribute to the impaired immune function resulting in increased preponderance of

infections in patients with chronic kidney disease[61]. Although any part of the body may be the focus of infection, urinary tract may act as a nidus of infection in many of chronic kidney disease patients. Infection of urinary tract may be a part of infection of renal parenchyma such as chronic pyelonephritis or due to secondary structural abnormality in urinary tract, obstructive uropathy, use of immunosuppressive agents, diabetes mellitus or catheterization. The contribution of uraemia in urinary tract infection is not known.

The present study was designed to prospectively assess whether uraemia or severity of chronic kidney disease per se in the absence of various predisposing factors results in higher incidence of urinary tract infection. In this study we compared the degree of leucocyturia and urinary tract infection in patients with chronic kidney disease and healthy population.

AIMS AND OBJECTIVES

1. To compare the incidence of UTI in chronic kidney disease patients and control population.
2. Age and sex distribution of urinary tract infection in chronic kidney disease patients and control population.
3. To map out the relationship between urinary tract infection and severity of chronic kidney disease.
4. Identification of uropathogens responsible for urinary tract infection in chronic kidney disease patients and control population.

REVIEW OF LITERATURE

HISTORICAL REVIEW

Individual cases of urinary tract infection were recorded in antiquity. For example, according to Asscher, there is little doubt that the reference to 'sending forth heat from bladder' in Egyptian papyri must have indicated the presence of infection. In Britain the first report of urinary tract infection appears to have been in 1412 by John of Ardenne.

Pasteur (1863) recognized urine as a good culture media for bacteria and Roberts (1881)[3] related the presence of bacteria in the urine to symptoms, but very little progress was made in exploring this relationship until quantitative assessments of the number of bacteria in the urine of patients with urinary tract infection were carried out by Marple(1941)[4] Barr and Rantz (1948)[5] and Sanford etal (1956)[6].

A comparison of catheter and Voided Specimens of urine allowed a distinction to be made between contamination with urethral or perineal bacteria (usually with gram positive cocci) and true infection of the bladder (usually with gram negative bacilli) Kass (1960)[7] Pfau and sacks (1970)[8]. Careful preparation of periurethral area before catheterization resulted in a

lower rate of contamination. Quantitative bacterial counting in both selected and unselected groups of the population showed that when the urine contained over 10^5 bacteriae/ml this could be regarded as true or significant bacteriuria (Kass 1955, 1956, 1957)[7]. Most patients with chemical infection had counts of 10^5 organisms per ml but even when there were no symptoms a few patients had bacterial counts of this magnitude. Thus the concept of symptomatic bacteriuria was established. Its association with the development of clinical infection and renal damage is well recognized.

Following World War II, several studies were conducted to study the exact relationship between renal failure and infection. Infection in the presence of other urinary tract lesions such as vesicoureteric reflux, calculus or analgesic abuse could accelerate the development of renal damage[9]. Reports began to appear suggesting that infection was a frequent complication of renal failure. (Bull and Merill)[10] stated that patients with renal failure were susceptible to infections.

PATHOGENESIS AND EPIDEMIOLOGY OF UTI:

Urine is normally a sterile body fluid. Presence of bacteria (bacteriuria) fungi (fungiuria) or virus is defined as infection. The term does not imply the presence or absence of associated symptoms.

Acute infections of the urinary tract based on anatomic categories.

Lower UTI – Urethritis and cystitis

Upper UTI – Acute pyelonephritis, Prostatitis, intrarenal and perinephric abscess

Chronic pyelonephritis refers to chronic interstitial nephritis from bacterial infection of the Kidney.

Epidemiologically UTI's are divided into catheter associated (Nosocomial) or non Catheter associated (Community acquired). Infections of either category may be symptomatic or asymptomatic.

UTI are unusual in male patients under the age of 50. Symptomatic infection is common among women between 20 and 50. Asymptomatic Bacteriuria is more common among elderly men and women.

UTI in adults can be categorized into six groups[12]

1. Acute uncomplicated cystitis in young women.
2. Recurrent acute uncomplicated cystitis in Young women.
3. Acute Uncomplicated pyelonephritis in young women.
4. Acute uncomplicated cystitis in adults with the following condition.
    - Male Sex
    - Elderly
    - Pregnancy

- Recent urinary tract instrumentation
- Childhood UTI
- Recent Antimicrobial use.
- Symptoms > 7 Days
- DM.

5) Complicated UTI[13]

a) Obstruction – Urolithiasis, Ureteric and urethral stricture, bladder diverticulas or Malignancy, urinary diversions.
b) Foreign bodies – indwelling catheter, ureteral stent, Nephrostomy tube
c) Functional abnormality – Neurogenic bladder, Vesicoureteric Reflux.
d) Others – RENAL FAILURE, Renal transplantation, Immunosuppression, Multidrug resistant, Uropathogen, Prostatitis related infection.

6) Asymptomatic Bacteriuria

Distinction between uncomplicated and complicated UTI is important mainly because of the necessity of evaluation of urinary tract and type and duration of antimicrobial treatment varies. Asymptomatic Bacteriuria in patients with complicated UTI like Renal failure, renal transplant, obstruction or neutropenia should require treatment.

Organism	Uncomplicated	Complicated[12]

Seven days of therapy with oral agents to which the organism is sensitive should be given. Long term therapy (4-6 weeks) may be necessary in high risk patients with persistent asymptomatic Bacteriuria. Asymptomatic Bacteriuria in immunosuppressive patients run an increased risk of bacteremia and hence it needs to be treated (MN Acharya etal)[13]

ETIOLOGY:

Most common agents are gramnegative bacilli Escherichia coli is by far the most frequent, cause of uncomplicated community acquired UTI'S[11]

G-Ve Organisms		
E-Coli	70-95	21-54
Proteus mirabilis	1-2	1-10
Klebsiella	1-2	1-17
Pseudomonas	< 1	2-19
Citrobacter	< 1	5
Enterobacter	< 1	2-10
Gram +ve organisms:		
Staph Saprophyticus	5-20	1-4
Enterococci	1-2	1-23
Group B Streptococci	< 1	1-14
Staph aureus	< 1	1-2

Route of infection:

Bacteria can invade and cause UTI via two major routes. Ascending and Hematogenous pathways.

Ascending infection is the most common route of infection in females. Ascent in association with urinary catheterization or cystoscopy is the most common cause of hospital acquired UTIS in both the sexes.

The high prevalence in females is because of short urethra (4 cm), close proximity to anus and its termination beneath the labia. Sexual intercourse causes introduction of bacteria into the bladder. Honey moon cystitis being a well recognized clinical entity in females. The relative infrequency of UTI in men may be attributed to the length of male urethra and bactericidal activity of prostatic fluid. The recurrent urinary symptoms in young and middle aged men may probably linked to prostatic dysfunction and in elderly male prostatic hypertrophy and changes in the residual volume of the bladder with reduced urineflow. Uterine prolapse increased the infection in elderly Women. With insertion of a urinary catheter the bacteria may be pushed along the urethra into the bladder or migrate along the track between the catheter and the urethral mucosa, gaining access to the bladder. Hematogenous spread (Descending Route) usually occurs as a result of baceteremia. Staphylococcus aureus or salmonella sp., candida albicans, Mycobaterium tuberculosis, leptospira sp., are common organisms.

PREDISPOSING FACTORS:

Obstruction to the flow of urine by anatomical or pathological abnormalities are major predisposing factors at any age.

SUGGESTED PRECIPITATING FACTORS IN THE DEVELOPMENT OF UTI

ANATOMICAL	CONGENITAL ABNORMALITIES
	PROSTATIC HYPERTROPHY
	CYSTOCELE, UTERINE PROLAPSE
	VUR.
PATHOLOGICAL	SURGICAL OPERATIONS ON THE UROGENITAL TRACT, TUMOURS OF BLADDER AND PROSTATE
	URETHRAL CATHETERIZATION
	SYSTEMIC ILLNESS – CKD, DM, ATROPHIC VAGINITIS
	NEUROLOGICAL DISORDERS OF BLADDER, IMMUNO SUPPRESSION.
INFECTIVE	VULVOVAGINITIS
	VAGINAL DISCHARGE
SOCIAL	SEXUAL INTERCOURSE
	MENSTRUATION
ENVIRONMENTAL	SEDENTARY OCCUPATION

Bacterial virulence:

Not all strains of E.coli are equally capable of infecting the intact urinary tract. Uropathogenic E-coli have

- Type 1fimbria that binds to uroepithelial cells
- Type P fimbriae

- α, β Hemolysins, cytotoxins that lyse erythrocyte capsule
- Siderophore for scavenging iron.

Geneticfactors: Maternal History of UTI are often found among women who had recurrent UTI.

MULTIPLICATION OF BACTERIA IN URINE

In the urinary tract there is a dynamic culture system in which bacteria undergo multiplication while urine is continuously being added by glomerular filtration and lost by micturition.

Normal urine unlike other body fluids does not contain significant quantities of lysozyme or immunoglobulin. Increased concentration of Ig A, IgG and IgM (Kaufman et al 1970)[14] (Burdon et al)[15] are found in adults with UTI. Phagocytosis of bacteria is impaired both by the absence of opsonin and the wide range of osmolality in urine (Chernew and Braude 1962)[16]. These considerations apply to urine alone, because mucosal defense mechanisms are highly active throughout the urinary tract.

The ability of urine to support bacterial growth is related to urinary PH, osmolality and chemical constituents such as glucose, amino acids and organic acids. Optimal bacterial growth occurs within a PH range of 6-7. Outside this range growth is either slowed or inhibited. The osmolality of the urine is an index of the concentrating ability of the Kidney. A lowered

osmolality encourages bacteriuria (Winverg 1959)[17](Katiz 1961)[18]; this is probably due to the associated presence of intrarenal infection, because eradication of this has been shown to correct the impairment of urinary concentrating ability (Norden and Tuttle 1965)[19].

Glucose provides a source of energy for the growth of urinary pathogenic bacteria and under experimental conditions prolongs the logarithmic phase of growth. The number of bacteria in the urine of diabetic patients was significantly higher than in that of non-diabetic controls (O' Sullivan et al 1961)[20] .Competitors of glucose utilization, 2deoxy –D.glucose and 6deoxy – D. glucose, reduce bacterial counts in urine (Weiser et al)[21]. Normal urine usually contains sufficient glucose to support maximal growth rates and any lowering of the PH is prevented by its buffering capacity.

The amino acid combination of urine may vary considerably; effects on bacterial growth have been noted. (Rooberts et al 1968)[22], but it is unlikely that these are important in urinary tract infection. Organic acids are also normally present in urine and may be bacteriostatic according to the degree of this dissociation. Urea in high concentration was shown to be bactericidal against urinary-tract pathogens (Schlegel et al 1961)[23], but it is likely that is effect is mainly due to an increase in osmolality because

bacterial inhibition also resulted from the addition of salts to give hyperosmolality.

DEFENSE MECHANISMS

Protection of the urinary tract against infections strongly related to the constant flow of urine and regular emptying of the bladder. Reduction in the regular flow of urine by for example, bladder-neck obstruction, prostatic hypertrophy or neurological disorders of bladder favors an increase in the number of bacteria and the development of infections. The efficiency of this hydrokinetic defense mechanism will depend on a balance of factors such as growth rate, the frequency of micturition, the urine flow from the kidneys, the residual volume of the bladder and the chemical composition of the urine and its ability to support bacterial growth.

The presence of Valvular structures in the urinary tract prevents or hinders the ascent of bacteria by reflux of urine. The uretero vesical valve is competent from both urine and bacteia by virtue of muscular structures (Tanago and Pugh 1963)[25] (Hutch 1972)[26] that permit a constant flow of urine from the ureter into the bladder (Stephens and Lenaghan 1962)[27] but prevent reflux when the bladder is full or during micturition . Any change that impairs the integrity of this musculature may result in a retrograde

flow of urine and leads to persistence of the infection by producing a ureteral residue (Edwards 1968)[28]. Complete emptying of the bladder tends to prevent infection, an excess of residual urine is commonly found in patients with recurrent infection (Hunman and Baumann 1973)[29],(Allen 1977)[30]. The urethro vesical valve is fluid competent but does not prevent the upward passage of bacteria into the bladder. They pass more easily up the female than up the longer male urethra and abnormal urodynamics may be more important in women than in man as a cause of recurrent infection (Lapides 1974)[31].

Mucosal defence against infection may result either from the phagocytic properties of inflammatory cells or from the secretion by mucosal cells of substances that inhibit the adhesion of bacteria or kill them (Vivaldi et al 1965)[32]. The urine contains many types of antibodies (Immunoglobulins) and these are considerably increased in amount when infection occurs in the tract. They may have protective role in the renal tissue, but in the urine no antibacterial activity has been established (Kaye 1968)[33]. An immune response occurs in adults and children with renal infection, as demonstrated by the production of serum antibodies to the somatic antigens of strains of E.Coli (Needell et al 1955)[34], (Pervical et al 1964)[35] , although (Wineberg et al 1963)[36] found a response only in association with lowered concentrating ability. These antibodies were

strain specific and would be of potential value only in recurrent infections due to the same strain. The various components of complements are either absent from urine or are inactivated by it (Beeson and Rowley 1959)[37]. Studies in experimental animals have supported a role for immunity in both renal and bladder infection (Arana et al 1965)[38]. Lehman et al 1968)[39], but immunization with somatic antigens to be specific virulence factors (Glyn et al 1971)[40] it gave only incomplete protection (Radford et al 1974)[41]

Prostatic secretions have been reported to have antibacterial activity in men. (stumey et al 1968)[42]. The antibacterial factor had shown to be zinc (fair et al 1976)[43]. Prostatic fluid zinc levels were considerably lower in men with chronic bacterial prostatitis than in normal men.

Significance of Bacteriuria:

In most patients growth of > 10^5 organisms or colony forming units (CFU) per ml from a properly collected **mid stream clean catch urine** sample indicated significant bacteriuria.

In symptomatic patients, suprapubic aspiration or sample collected from indwelling catcheter colony counts of 10^2-10^4/ml generally indicate infection.

In Asymptomatic patients two consecutive urine specimens with colony counts of > 10^5 bacteria of single species per ml should be demonstrable in both the specimens before initiating therapy. In complicated UTI colony count threshold of >10^3 CFU/ml is used to diagnose infection as per Infections Disease society of America consensus; but concomitant significant pyuria (Presence of 8 or more leucocytes per cubic mm on microscopic exam of uncentrifuged urine) should be present.

CHRONIC KIDNEY DISEASE:

It is defined as either Kidney damage or Glomerular filtration rate <60 ml/mt/1.73 m^2 for 3 or more months. Kidney damage is defined as pathologic abnormalities or markers of damage including abnormalities in blood, urine tests or imaging studies[45].

The National Kidney foundation (Kidney dialysis outcomes quality intitative KDOQI) provides stages of chronic Kidney disease according to estimated GFR[45].

STAGE	**DESCRIPTION**	**GFR (ml/mt/1.73m^2)**	**ACTION**
I	Kidney damage	> 90	Diagnosis,

	with normal or ↑GFR		treatment, cardiovascular disease-risk reduction
II	Kidney damage with mildly ↓GFR	60-89	Estimate progression
III	Moderately ↓GFR	30-59	Evaluate and treat complication
IV	Severely ↓GFR	15-29	Prepare for Renal Replacement therapy (RRT)
V	Kidney failure	< 15 Or Dialysis	RRT
V	Uraemic Emergency or ESRD	< 5	hyperkalemia, pulm edema, pericarditis Encephalopathy warrants emergency Dialysis..

The term chronic renal failure applies to the process of continuing significant irreversible reduction in nephron number and corresponds to CKD stage 3-5 .The term End stage Renal Disease (ESRD) represents a stage where the accumulation of toxins, fluid and electrolytes normally excreted by the Kidneys result in the uraemic syndrome. It corresponds to stage 5 with uraemic emergencies.

Glomerular Filtration Rate (GFR)[46]

Two Equations are commonly used to estimate GFR, Using serum creatinine Age, sex, race and Body weight.

The normal annual mean decline in GFR with age from the peak GFR (120 ml/mt/1.73 m^2) starts from the 3rd decade. It reaches a mean value of 70 ml/mt at 70 yrs. The mean GFR is lower in women than men.

1. Cockcroft – Gault Equation:

Estimated GFR (ml/mt)

$$= \frac{(140 - \text{age}) \times \text{Body wt in Kg}}{72 \times \text{serum creatinine (mg/dl)}}$$

Multiply by 0.85 for women.

2. Modification of Diet in Renal Disease study Formula. (MDRD)

$$GFR = 1.86 \times (\text{Plasma creatinine})^{-1.154} \times (\text{AGE})^{-0.203}$$

Multiply by 0.742 for women

Multiply by 1.21 for African Americans.

We adopt cockcroft Gault formula to estimate GFR in this study.

Minimising Progression in CKD:

Delaying or preventing progression of kidney failure is a priority in the Management of any CKD patients.

Some of the causes for acute on CKD:

1. **Infection.**
2. Dehydration
3. Nephrotoxic drugs- NSAIDS, ACEI, ARB etc.
4. Accelerated Hypertension
5. Urinary tract obstruction.
6. Heart failure, Hypotension – compromise renal perfusion

Morbidity and mortality remain high in Patients with CKD predominantly due to infections and cardiovascular complications. The incidence rate of sepsis, urinary tract infection (UTI) and pneumonia in patients with and without CKD were reported from medicare patients in 1998 by Anne murrray MD. Of minneapolis minnesota[47]. Most patients had stage 3 CKD. There was 2-3 fold increased risk of sepsis UTI and pneumonia in patients with CKD. The mortality rate in CKD patients with one of these infections was 1.5-2 times greater in CKD patients compared with non CKD patients. The rates of bacteremia or UTI were similar in HD and PD patients.

URINARY TRACT INFECTION IN CKD

Patients with CKD have an increased susceptibility to infection. Septicemia is commonly a complication of UTI in CKD. The same organism can be cultured from urine and blood[48]. The urinary tract constitutes a frequent source of infection in these patients. Multiple factors may be responsible for the increased incidence of UTI such as suppression of various aspects of immune system, azotemia, infrequent voiding, low urinary flow rate and urinary concentration defects.

MECHANISMS RESPONSIBLE FOR INFECTION IN CKD

A number of separate mechanisms of host defence may be impaired in renal failure.

1. HOST DEFENSES IN RENAL FAILURE

It is difficult to discuss susceptibility of the host except in terms of a specific parasite. The approach to this problem is a description of an infectious disease by its location stresses the importance of alternation of the local defence mechanisms which increases susceptibility to infection in renal failure.

A. LOCAL BARRIERS TO INFECTION

Intact skin and mucous membrane are frequently damaged in patients with renal failure. The alternation of natural barriers, trauma to skin and mucous membrane has part of the natural history of renal failure. Urinary catheterization and other measures repeatedly break mucosal barriers. Each of this manoeuvers is a potential threat to the patient.

B. INFLAMMATORY RESPONSE AND PHAGOCYTOSIS

Limited evidence suggests that the host is incapable of a normal inflammatory reaction in renal failure (Blach and Evans). A lesser inflammatory response to infection of monosodium urate in patients with CKD was noted by (Buchman et al)[49].

Renal failure may influence different aspects of inflammatory response eg; migration of granulocyte was found to be reduced in patients with renal failure and acidosis. A direct metabolic effect of acidosis on granulocyte may be responsible since similar effect and other altered granulocyte function were seen in diabetic patients with DKA. The influence of osmolality could interfere with the actions of phagocytes. Increased osmolality of the suspending solution inhibited phagocytosis and intracellular killing of bacteria in vitro.

Leukocytes pyrogen probably plays an important role in local inflammation and also in systemic response to infection. Potassium has been shown to influence the release of pyrogen & it is possible to speculate that raised K level or other blood electrolyte changes alter the fever and inflammatory response in renal failure by these means.

C. IMMUNE MECHANISM

HUMORAL: A clinical study has demonstrated that humoral antibody production may be impaired in CKD. Wilson et al[50] measured the response to typhoid vaccine in 10 patients with CKD and 22 normal subjects. Patients with renal failure had a reduced reponse to O & H antigen. Other components of serum concerned with immune mechanism have been examined in renal failure. Serum complement levels and alpha globulin have been found to be normal in patients with CKD although reduced properdin levels have been noted.

CELLULAR: Experiments in recent clinical trials have been shown a suppression of cell mediated delayed hypersensitivity reaction in CKD, The mechanism of prolonged survival of homograft in renal failure aptly called nature's immunosuppressive device by Lawrence has been long studied. There is evidence which suggests that the reaction of lymphoid tissue is altered in renal failure. (Burewell et al)[51]

Changes in lymph nodes were noted in patients with CKD by mutirhead & Shields[52] Black and Chaborn[53] found that axillary lymph nodes from 34 patients with renal failure showed dilated sinusoids that contain erythrophagocytic histiocyte in loose syncitial arrangements. Plasma cells, eosinophils and Secondary follicles were typically absent in these lymph nodes when compared with control subjects. The absence of secondary follicles suggested that there was an impaired responsiveness of the lymph nodes of patients with CKD Black and Chaborn[53] commented that this was particularly notable because many of these patients died with intercurrent infection when secondary follicles should have been prominent in lymph nodes. Wilson et al also noted that thymus gland removed from subjects with renal failure were atrophic. He also suggested that there was impairment in the formation of cells containing cell bound antibody (or cells forming humoral antibody). Lymphopenia in renal failure adds other evidence of altered lymphoid tissue.

II. FACTORS RESPONSIBLE FOR ALTERED HOST DEFENCES

A. TOXIC AGENTS:

Many substances excreted in urine and which accumulates in the body in renal failure (Phenol, indole, aromatic acids) has been shown to have profound effects. Serum from patients with renal failure was found to

inhibit serum enzymes in vitro and similarly (Hicks et al)[54] showed that many aromatic acids that accumulate in CKD depress the reaction rate of enzymes. (Marksin & Rewice)[55] noted that that maturation of normoblastin tissure cultures of bone marrow was inhibited by uraemic serum. Protein synthesis was inhibited by uremic serum. Protein synthesis was inhibited by compounds isolated from patients with CKD. Urea has also been shown to interface with Antigen Antibody reaction. Although the concentration of urea required producing these effects are usually considerably in excess of those found in renal failure. It has been found that urea in concentration as low as 0.05 M inhibits Monoamine oxidase.

B. ACIDOSIS

Dubos who formulated the hypothesis that factors activating infections operate through common pathways, stressed the significance of metabolic state in host parasite equilibrium.

The importance of H+ ion concentration in acute inflammation, the action of reticulo endothelium system, bacterial proliferation and the antimicrobial activity of tissues. Metabolic acidosis has usually impaired host defenses in studies conducted. The delayed appearance of leucocytes at an inflammatory site and the impaired phagocytic function have been described in patients with renal failure and diabetes mellitus. Shreiner &

Mahar[56] Speculate about the possibility that intracellular K^+ deficiencies occurring as a result of renal failure may account for an increased susceptibility to infection. The histological changes in renal tubules that follow this increased the susceptibility to pyelonephritis. Change in PH influences the bactericidal action of serum. Chronic acidosis also may result in reduced collagen formation and poor wound healing thus perpetuating infection, thus in patients where the PH of inflammatory exudates is considerably less as such when compared to blood, further lowering of PH may be an important determinant in the host- parasite relationship in renal failure.

C. MALNUTRITION

Patients in chronic Kidney Disease are usually undernourished as a result of nausea, vomiting and unattractive lowprotein diets. It is difficult to correlate resistance of infection with malnutrition. Although increased susceptibility to infection in children with Nephrotic syndrome is well recognized and has been assumed to result from low levels of serum gamma globulin, it is not clear whether the degree of protein deficiency in CKD which is insufficient to alter measurable protein levels in the blood can account for increased susceptibility to infection.

D. CORTICOSTEROIDS

The striking similarities between effects of renal failure and the action corticosteroids has led to the speculation that failure may produce some effect like prolonged homograft survival, reduced fever reaction and inhibition of protein synthesis. Elevated levels of 17 hydro corticosteroid often reported in patients with chronic kidney Disease appears to depend mainly on the reduced clearance by the damaged kidney and the changes are reversible. These elevated 17 hydroxy corticosteroids may play a role in increased susceptibility to infection.

DIAGNOSIS OF UTI

SYMPTOMATOLOGY AND CLINICAL FORMS OF UTI

Symptoms of lower urinary tract infection include dysuria frequency&urgency, strangury, hematuria and suprapubic pain, but in many patients significant baceriuria may be present without symptoms. Diagnosis based on symptoms alone is highly inaccurate with a 50% of false negative rate.

Definitions of some of the urinary symptoms:

Dysuria – Pain immediately before, during or after micturition.

Urgency- Loss of normal ability to postpone micturition.

Frequency- Frequent voiding results from reduction of functional bladder capacity or bladder and urethra irritation.

Strangury: Unpleasant and painful desire to void when the bladder is empty or nearly so.

Clinical forms of urinary tract infection:

1.Cystitis:

Usually report dysuria, frequency, urgency and suprapubic pain.

Urine is cloudy and malodorous or bloody. physical examination reveals tenderness over suprapubic area.

2. Acute urethral syndrome:

Patients are young, sexually active women, Dysuria, frequency or urgency with colony counts, 10^5 cfu/ml in urinary culture. Chlamydia, N. Gonorrhoeae, or anaerobic infections account for some cases.

3. Acute Pyelonephritis:

Fever, chills, rigor, abdominal pain, nausea, vomiting or diarrhoea may be present.

Physical examination reveals tenderness on deep pressure over one or both. Costovertebral angle.

Persistence of fever or symptoms beyond 72 hrs after appropriate antibiotics warrants urological imaging

4. **Infection associated with bladder dysfunction**

Neurological disorders of spinal cord, multiple sclerosis or CVA, malignancy of bladder and prostate and disturbances following surgical procedures also may affect the urine flow and often necessitate catheterization. Often specimen collection is difficult and organisms present frequently show multiple drug resistance. Bacteriuria should always be confirmed but treatment should be considered, only when there are constitutional symptoms or difficulty in maintaining freedrainage. Intravesical wash out with antiseptic or antimicrobial agents may be the best treatment.

5. Infection in diabetics

UTI is 2-3 times more common in adult diabetic patients than in non diabetics. Failure to control blood sugar may be contributory factor and this group is particularly predisposed to develop acute pyelonephritis and renal papillary necrosis. Bacterial counts tend to be high in diabetic urine because of increased glucose content.

Emphysematous pyelonephritis:

It occurs almost, always in diabetic patients. It is characterised by a rapid progressive course with high fever, leucocytosis, and renal parenchymal necrosis accumulation of fermentative gases in the kidney

and perinephric tissues. Most patients have significant pyuria. E coli cause most cases. Enterobactericeae causes some cases. Gas is seen on plain films but confirmed by CT scan. Appropriate antibiotics with surgical resection of the involved tissue are warranted. It carries high mortality.

6. Bacteriuria of pregnancy

The prevalence of bacteriuria in pregnant women may rise to 10% at term. Increase in parity and a past history of UTI significantly increases the likelihood of bacteriuria. Prematurity, low birth weight and fetal mortality appear to be increased reflecting past or recurrent UTI, current renal abnormalities or diseases. The association of acute pyelonephritis together with other risk factors justifies urinary screening for antenatal bacteriuria.

7. Bacterial prostatitis:

In young men, prostatic infection causes frequency, dysuria, perineal or testicular pain and in acute cases myalgia and fever. If prostatic fluid is available a microscopical and bacteriological culture can be carried out. The diagnosis is best made by the stamey test. In all cases significant bacteriuria may be present. Though in chronic infection the count is low

but significant eradication is difficult due to difficult penetration by anti microbial into prostate.

8. **Others**

Genito urinary TB - The presence of persistent sterile pyuria and culture of TB bacilli offers diagnosis.

Viruses are not very common as causative agents. Fungal infections are important in immunocompromised. Parasitic infections of the urinary tract may led to various pathological lesion. Eg: Schistosomiasis, Trypanosomiasis, Filariasis & Hydatid disease.

CRITERIA FOR CLASSIFICATION OF UTI:

S.No	Category	Clinical	Laboratory
1.	Acute Uncomplicated UTI in women	Dysuria, urgency frequency, suprapubic pain no fever or flank pain	> 10 WBC / mm3 > 10^3 CFU /ml of uropathogens in mid stream clean catch urine.

2.	Acute Uncomplicated pyelonephritis	Fever with chills, flank pain	> 10 WBC /mm3 > 10^4 CFU /ml of uropathogen in mid stream clean catch urine.
3.	Complicated UTI and UTI in men	Any combination of symptoms Factors associated with complicated UTI.	> 10 WBC/mm3 > 10^5 CFU /ml of uropathogen in mid stream clear catch urine.
4.	Asymptomatic bacteriuria	No urinary symptoms	> 10 WBC /mm3 > 10^5 CFU /ml in two consecutive mid stream clean catch urine > 24 hrs apart.

SPECIMEN COLLECTION

Various methods may be used for the collection of urine specimen. Volume of urine collected varies depending upon the suspected pathogens and kind of processing necessary for isolation. The minimal acceptable volume when bacterial pathogens are suspected is about 0.5 to 1 ml. However at least 3 ml must be collected preferably.

Methods used to collect urine specimen

- Suprapubic aspiration
- Mid stream clean void
- Midstream void
- Uncleansed initial – void
- In and out (or straight) catheterization.
- Use of indwelling catheter.
- Use of suprapubic catheter.
- Use of external collection device.
- Use of ileal conduit.
- Cystoscopy.

Midstream clean void method

For both males and females, **the mid stream clean voided or clean catch specimen** is most often recommended. The method is non invasive and with good instruction yields an adequate specimen for microbiological examination. In females adequate periurethral washing before sampling results in fewer positive cultures.

In preparation for collection of a clean voided specimen, the patient is asked to wash hands dry. The female patient is instructed to clean the urethral meatus thoroughly after separate in labia. Keeping the labia spread she should begin to void. In males also the urethral meatus should be washed thoroughly after retracting the foreskin if he is uncircumcised and then void. The patent should discard the initial portion of urine about (15-30 ml) in the toilet. Then aseptically a specimen of urine should be collected in a sterile container.

Specimen transport:

The proper handling and transport of urinary specimens are crucial to obtaining reliable information. Specimens transported without a preservative must be cultured within 1–2 hours, or else cooled immediately at 4°C. This refrigeration is necessary to prevent rapid logarithmic phase growth which can leads to spurious increase in CFU/ml. If refrigerated, specimens should be stored for not more than 24 hours. Refrigeration does not preserve WBCs very well. Frozen specimens are unacceptable for culture and should be rejected. The FLORASTAT URINE TRANSPORTING System is a newly developed lyophilized transport system that seems to be able to stabilize, microbial population for 24 hours at room temperature even in the presence of antibiotics[57].

Microbiology of UTI

E.Coli is the commonest cause of UTI and is found in about 90% of uncomplicated infections is general population and 50% of hospital acquired infection. Other primary pathogens include proteus mirabilis which is a common cause of UTI in boys and men and is associated with renal abnormalities particularly calculi. Proteus species may cause chronic UTI in association with obstruction or use of instruments. Streptococci are seldom primary pathogens and urinary tract enterococci are often found as contaminants in UTI. Group B streptococci appear to be occasional primary pathogen in women. Staph. Epidermidis and micrococci are part of normal skin flora and often found as contaminated in urine. The novobiocin resistant staph. Saprophyticus is a true primary pathogen of urinary tract.

In the complicated UTI that occur particularly in hospital patients, E.Coli is still the commonest causative organism. But other members of enterobacteriaceae such as klebsiella, enterobacter, indole positive proteus and citrobacter are also frequent. UTI due to streptococcus fecalis are usually associated with the use of instruments or catheterization. Pseudomonas aeruginosa infections associated with major structural or physiological abnormalities of urinary tract or permanent urethral catheterization. Staph. Aureus is uncommon and almost invariably

associated with localized lesions of kidney or is secondary to prostatectomy or catheterization. The role of anaerobes and other fastidious bacteria is doubtful.

Laboratory methods:

Examination of the urine will include microscopy, chemical examination and quantitative culture. The purpose of microscopy is to determine the numbers of white cells, but an increase (pyuria) does not necessarily indicate the presence of in inflammation. Pyuria is present in most clinical infections but may be absent in symptomless bacteriuria. Gross contamination of the urine with white cells may occur where there is a genital tract infection or urethritis. Urethral catheterization may increase the number of white cells in the urine. Pyuria without bacteriuria may be an indication of tuberculosis. The excretion of white cells is variable and results obtained on a single specimen of urine may be highly misleading. A better assessment is obtainable from a timed 4 or 6 hour excretion. Microscopy will also reveal the presence of urinary casts, red cells, renal tubular cells or atypical cells which may indicate non-infective renal pathology. White cells and bacteria seen in gram stained films of the urinary deposit may have come from the genital tract.

Methods of detecting bacteriuria and pyuria

Cultural	* Quantitative	Pour-plate technique.
		Surface viable count
	* Semiquantitative	Standard loop (streak)
		Filter – paper method
		Dip-spoon
		Dip-slide
		Agar-cup
		Roller tube
		Pad culture
		Swab culture
Chemical		Griess nitrate
		Tetrazolium chloride (TTC)
		Glucose oxidase
		Catalase
White Cells		Quantitative count
		Leucocyte esterase
Bacteria		Gram's stain
		Bac – T – Screen
Automated		Photo metry (turbidity)
		Bioluminescence (ATP assay)
		Electrical impedance
		Limulus – ameobocyte assay (endotoxin)
		Micro calimetry (heat production)
		Coulter counter (particle size)
		Radiometry (**BACTEC**, Carbon 14)

Pour Plate Method: (Quantitative)

This method yields a quantitative culture of urine, in which serial dilutions of urine specimen are incorporate into 50°C agars, which is then mixed and poured into plates. The medium is allowed to solidify and incubate at 35°C for 24 hours. This time consuming process allows the enumeration of bacteria based on the dilution factor.

Surface streak procedure (Semiquantitative):

Semi quantitative cultures are carried out in a standardized fashion by using the surface streak procedure for delivering a measure volume of well mixed urine on to an agar surface. To ensure accuracy a vertically held calibrated loop must be dipped quickly and without specimen carryover on the shank. The calibrated loop is used to streak a straight line down the middle of the agar surface.

The agar surface is then cross-stretched for isolated colonies. Inoculation with a 0.001 ml loop will permit detection of lower counts. To determine the member of CFU/ml in the original specimen the number of CFU detected after incubation is multiplied by 1000 if a 0.001 ml loop was used.

Media used are a standard combination of a nonselective and selective agar for gram-negative bacilli. Agar plates are usually incubated at 35-37°C under aerobic conditions in normal situations. Generally 18-24 hrs incubations is sufficient, except for fastidious organisms and isolates from patients on antimicrobial therapy which require longer periods of incubation.

Various techniques are available for determining the susceptibility of urinary pathogens to antimicrobial agents. Methods in general use are the Impregnated Disc, Break Point and Minimum Inhibitory Concentration Tests.

Principles for treatment:

Asymptomatic patients usually do not require treatment since spontaneous remission is common. However pregnant woman, diabetics or patients for surgery and instrumentation require treatment due to the risk of serious complications. Antimicrobial therapy should be tailored to needs of the individual patient but two major principles must be followed.

1. Dose of the antimicrobial agent should produce therapeutic concentration at the infection site.
2. The course of treatment should be only as long as in necessary to achieve the defined effect, to minimize ill effects of bacterial resistance, superinfection and drug toxicity.

In acute simple infections a three day short course is usually sufficient and acceptably to patients, especially in uncomplicated UTI.

In complicated UTI which may show pathogens with resistance, a prolonged course and higher doses (particularly when renal involvement is present) are needed.

S.No	Treatment regimens	Empirical Treatment
1.	Acute uncomplicated cystitis in women	3 day regimen ORAL: Trimethoprim & sulfamethoxasons 160/800. q12 h quinolone or Norfloxacin 400 mg BD,

		Ofloxacin 200 mg BD. Diabetic, pregnant women 7 days.
2.	Acute uncomplicated pyelonephritis in women	ORAL quinolone 7 -14 days. (or) Single dose Inj. ceftriaxone (1g), Gentamicin 3-5 mg/kg IV followed by ORAL, Trimethoprim – SMX 14 days
3.	Complicated UTI in men & women	Mild – ORAL Quinolone for 10-14 days Severe (Urosepsis) – Parenteral ampicillin + Gentamicin, Ceftriaxone, Imipenam /cilastatin then Oral quinolone or TMP/SMX for 10-21 days.

MATERIALS AND METHODS

A total of fifty patients aged 15 – 65 years having chronic kidney disease of varying severity attending the Nephrology and Medicine departments in Thanjavur Medical College Hospital, Thanjavur were studied (group) with in a period of 1 year from December 2009 to November 2010. Based on estimated GFR, Chronic Kidney Disease of stage 3 to 5 are included in the study. Group B consists of 50 age and sex matched control which included those who came for master health check up and healthy bystanders of patients.

Exclusion criteria:

1. Patients having infection related renal disease such as chronic pyelonephritis.
2. Diabetes mellitus
3. Patients on immunosuppressive drugs.
4. Indwelling or recent urinary catheterization
5. Urinary tract obstruction (urethral stricture, prostatic enlargement renal or ureteric calculi) or ADPKD
6. Patients on antimicrobials at the time of the study or within one week of the study.
7. Patients with HIV infection.

Detailed history was taken with particular emphasis on dysuria, urgency, frequency, abdominal pain, fever with chills, abdominal distension. Pedal edema and oliguria (oliguria refers to a 24 hours urine output of < 400 ml). Past history of hypertension and renal failure of more than 3 months were noted.

This was followed by detailed general examination. The presence of pallor, abdominal distension and pedal edema were looked for. The pulse, blood pressure and body weight were recorded and detailed systemic examination was carried out.

An elaborate laboratory examination of cases which included

- Complete hemogram
- Blood sugar
- Blood urea
- Serum creatinine
- Serum electrolytes
- USG abdomen[62]
    - The normal size of the kidneys are 10-13cm x 5-7cm.
    - In chronic kidney disease
        - Both kidneys are shrunken in size.
        - Hyper echoic cortex compared with liver
        - Cortical thickness is reduced
        - Cortico medullary differentiation (CMD) is lost.

All the cases and controls were subjected to urine examination for albumin, sugar and leukocytes, as well as culture and antibiotic sensitivity testing.

For microscopic examination of urine a clean catch urine sample was used. Urine specimen was examined within 1 – 3 hrs to avoid lysis of cells and casts. Centrifuged samples were used and leukocytes were counted under high power field and expressed as average number of leukocytes per HPF.

Urine culture was done by collecting mid stream clean catch urine specimen in autoclaved container. These were immediately plated on appropriate agars with graduated loops, incubated over night and examined. Results were expressed as colony forming unit (CFU) per ml of urine. All the bacterial isolates were identified by standard bacteriological techniques. Antibiotic susceptibility was also tested.

Symptomatic was defined as one having dysuria, frequency, urgency, abdominal pain associated with fever with chills and rigor.

Significant bacteriuria was defined as bacterial count greater than or equal to 10^5 CFU/ml of urine on two consecutive specimens in asymptomatic individuals or on culture of $\geq 10^5$ CFU/ml of urine accompanied by signs and symptoms of UTI. Contamination of urine was suspected if 3 or more micro organisms were grown simultaneously in culture.

Significant pyuria was defined as > 8 – 10 WBC per HPF in centrifuged specimens.

Urinary tract infection was defined as simultaneous presence of significant Pyuria and Bacteriuria.

OBSERVATION AND RESULTS

Table – 1

AGE DISTRIBUTION

AGE IN YEARS	STUDY (GROUP A)	CONTROL (GROUP B)	PERCENTAGE OF UTI	
			STUDY	CONTROL
15-24	3	4	-	-
25-34	5	4	20%	-
35-44	13	13	7.69%	7.69%
45-54	17	17	17.6%	-
55-64	10	10	20%	-
≥ 65	2	2	-	-
TOTAL	50	50	-	-

TABLE II

AVERAGE AGE OF UTI

	STUDY (GROUP A)	**CONTROL (GROUP B)**
MEAN AGE	45.22 Yrs.	45.4 Yrs.
MEDIAN AGE	45.5 Yrs.	46 Yrs.
% OF UTI IN YOUNG AGE GROUP (15-44 Yrs.)	9.5%	4.76%
% OF UTI IN OLD AGE GROUP (45-65 Yrs.)	17.2%	-

TABLE III

SEX DISTRIBUTION

AGE GROUP	STUDY (GROUP A)		CONTROL (GROUP B)	
	MALE	FEMALE	MALE	FEMALE
15-24 Yrs	1	2	3	1
25-34 Yrs	2	3	3	1
35 -44 Yrs	8	5	7	6
45-54 Yrs	11	6	11	6
55-64 Yrs	8	2	6	4
≥ 65 Yrs	2	-	1	1
TOTAL	32	18	31	19

TABLE IV

% OF UTI ACCORDING TO SEX DISTRIBUTION

AGE GROUP	PERCENTAGE OF UTI			
	STUDY (GROUP A)		STUDY (GROUP B)	
	MALE %/(n)	FEMALE %/(n)	MALE %/(n)	FEMALE %/(n)
15-24 Yrs	-	-	-	-
25-34 Yrs	-	33.3% (1)	-	-
35-44 Yrs	12.4% (1)	-	-	16.6% (1)
45-54 Yrs	18.18% (2)	16.6% (1)	-	-
55-64 Yrs	25% (2)	-	-	-
≥ 65 Yrs	-	-	-	-
TOTAL	15.6%	11.11%	-	5.2%

TABLE V

CORRELATION BETWEEN SIGNIFICANT BACTERIURIA AND PYURIA WITH UTI, IN CKD AND CONTROL GROUPS

IN STUDY GROUP A

AGE GROUP	NUMBER OF PATIENTS	SIGN. BACTERIURIA (n/%)	SIGN. PYURIA (n/%)	UTI (n/%)	SYMPT. UTI	ASYMPT UTI
15-44 Yrs	21	3 (14.25%)	3 (14.28%)	2 (9.5%)	1 (20%)	1 (5.5%)
45-65 Yrs	29	9 (31.03%)	5 (17.24%)	5 (17.2%)	3 (27.2%)	2 (12.5%)
TOTAL	50	12 (24%)	8 (16%)	7 (14%)	4 (25%)	3 (8.8%)

TABLE VI

IN CONTROL GROUP B

AGE GROUP	NUMBER OF PATIENTS	SIGN. BACTERIURIA (n/%)	SIGN. PYURIA (n/%)	UTI (n/%)	SYMPT. UTI	ASYMPT UTI
15-44 Yrs	21	1 (4.76%)	1 (4.76%)	1 (4.76%)	1	-
45-65 Yrs	29	1 (3.44%)	-	-	-	-
TOTAL	50	2 (4%)	1 (2%)	1 (2%)	1 (33.3%)	-

TABLE VII

UTI IN RELATION TO CKD IN TERMS OF SEVERITY

	CHRONIC KIDNEY DISEASE		
	STAGE III **GFR 30 – 59**	**STAGE IV** **GFT 15 – 29**	**STAGE V** **GFR < 15**
Number of Patients (n / %)	7 (14%)	29 (58%)	14 (28%)
(n / %) UTI	-	2 (6.89%)	5 (35.71%)

Chi square – X_2 5.75 P value < 0.01

TABLE VIII

UROPATHOGENS IDENTIFIED IN CKD PATIENTS

ORGANISM	NO.OF CASES/ %	SIGN. PYURIA	SIGN. BACTERIURIA	UTI (n/%)
E.Coli	11 (22%)	7	9	6 (12%)
Klebsiella	3 (6%)	-	2	-
Pseudomonas	1 (2%)	1	1	1 (2%)
Proteus	1 (2%)	-	-	-
Enterococcus	-	-	-	-
Staphylococcus	-	-	-	-
TOTAL	16 (32%)	8 (16%)	12 (24%)	7 (14%)

ANALYSIS AND DISCUSSION

AGE AND SEX DISTRIBUTION OF UTI

The age of the patients varied from 15 to 65 years in the study. The means age of group A CKD was 45.22 yrs and the median age was 45.5 yrs. The study group comprised 32 males and 18 females (64 percentage and 36 percentage respectively).

In comparison the group B (control) consisted 50 age and sex matched persons, comprising 31 males and 19 females (62% and 38% respectively) The mean age of this group was 45.4 yrs and the median age was 46 yrs.

Among CKD patients the incidence of UTI in the older age group 45 to 65 yrs was higher (17.2%) compared to the younger population between 15 to 45 yrs (9.5%). On comparing the incidence of UTI in the two sexes in CKD group, the incidence was (15.6%) in males and (11.1%) in females.

Amongst the controls none of the 31 males had UTI while (5.2%) of females had UTI. In our study males had more UTI than females in CKD whereas in control group females were more affected. In a study by

Gauba et al (1997)[2] males with CKD had higher incidence (14.2%) than females (8.1%).

SYMPTOMATOLOGY

Of the 50 patients in Group A 16 patients (32%) presented with symptoms of UTI. Most common symptoms were dysuria, increased frequency, urgency of micturition and lower abdominal pain. Among the CKD patients having symptoms suggestive of UTI, 25% were found to have UTI whereas among the asymptomatic patients 8.8% had UTI. Of the control with symptoms of UTI, 33.3% had UTI while none of the asymptomatic persons had UTI.

In our study, the CKD group showed a higher incidence of asymptomatic infection as opposed to control group, where only symptomatic infection was observed. Choudhry et al (1993)[58] suggested that patients with end stage renal disease with their defective host defence mechanism and those with low urine volume and urine stasis are at higher risk of asymptomatic UTI.

SIGNIFICANT BACTERIURIA AND PYURIA

The incidence of significant pyuria (8-10 pus cells /HPF) was 16% in patients with CKD whereas significant bacteriuria and UTI were (24%)

and (14%) respectively. In comparison, among the control subjects the incidence of significant pyuria was (2%), significant bacteriuria and UTI were (4%) and (2%) respectively.

In a study by (Montogomerire et al)[48] 60% that is 49/81 patients with CKD developed various infection. In these patients if chronic pyelonephritis was excluded, 44% had UTI which was exceeded only by pulmonary infections. In a study by Annemurray et al there was 2-3 fold increased risk of sepsis, UTI and pneumonia in patients with CKD[47].

Saitosh et al[58] reported an incidence of 27% of bacteriuria 38% of pyuria and 19% UTI in 182 oliguric patients with CKD. Collins AJ United States renal data system[59] also supports this. Mehr and associates[61] reported the 27 of the 62 patients (44%) had bacteriuria and / or innumerable leukocytes in the urine sediments.

The incidence of UTI among CKD patients is 14% and 2% in Control population. **The difference in proportion is significant (P< 0.05; Z = 2.27).**

The proportion of bacteriuria among CKD patients is 24% and among control is 4%. **The difference in proportion is highly significant (P<0.001: Z= 3.009)**

The proportion of pyuria among CKD patients is 16% and among control group is 2%. **The difference is significant (P<0.05: Z=2.54)**

SEVERITY OF CKD AND UTI

The incidence of UTI increased with severity of CKD. It was found that incidence of UTI in stage 4 and stage 5 were 6.89% and 35.71% respectively, where as in stage3 there was no positive case for UTI. **The incidence of UTI is increased with the severity of CKD significantly. CHI square X_2 5.75, P < 0.01**.

In the study by Gauba et al [2] they found that in patients with mild and moderate CKD the incidence of UTI was 6.6% and 8.7% respectively, where as 47% of the patients with severe CKD had evidence of UTI.

Similarly the daily urine output also appeared to have an influence on the incidence of UTI. The incidence of infection with urine output of 400ml or less per day had (3.14%) incidence of UTI. Friedman and Gladstone(60) reported the effects of hydration and bladder incubation time on urine colony count. Fault reported that confirmation of the diagnosis of UTI raised obvious difficulties in patients with little or no urine output. He stated that patients whose urine output is only a few ml per day capable of producing a clean catch sample for culture as also that a

single voided samples are enough for diagnosis in patients whose urine output was only few ml per day.

According to (saitosh et al [58]) pyuria is associated with decreased urine output and was frequent in oliguric patients.

In our study, among 21 oliguric patients 7 showed significant pyuria(33.3%) and 11 showed significant bacteriuria (52.3%). In nonoliguric patients the incidence of both significant bacteriuria and pyuria was (3.47%).

UROPATHOGENS

In the present study gram negative organisms were identified most frequently. **E.Coli** was the most prevalent organism and it contributed 85.7% as the causative organism of UTI in CKD patients, followed by **pseudomonas** (14.35%)

In the study by us 16 positive urine culture was obtained from the CKD group of which 11 was by E.Coli (68.75%), 3 by Klebsiella (18.75%), I by proteus and pseudomonas each (6.25%% each). According to study by saitosh et al[59] E.Coli Pseudomonas and Klebsiella contributed 40%, 10% and 12% respectively as causative organisms of UTI in CKD patients. They got 50 positive urine culture out of 184 patients of which 40% was by E.Coli 10% by pseudomonas, 12% by Klebsiella and 30% by

enterococcus. Gauba et al[2] in his studies obtained gram negative organisms in the majority (83.3%) of patients with UTI in CKD. E.Coli was the most prevalent organism and caused UTI in about 50% of cases, followed by Klebsiella (16.6%) and Pseudomonas (8.3%).

Among the 50 controls in our study one had UTI. Among the 31 males none had UTI while one out of 19 females had UTI E.Coli was the organism identified.

The ratio between incidence of UTI among patients with CKD and incidence of UTI among control population is 7 (relative risk). Hence ***the patients with CKD seven times more prone to develop UTI when compared to normal population.***

CONCLUSION

1. **THE INCIDENCE OF UTI AMONG CKD PATIENTS AT THANJAVUR MEDICAL COLLEGE, THANJAVUR WAS FOUND TO BE 14/100 PATIENTS (ONE IN SEVEN PATIENTS).**
2. **THE INCIDENCE OF UTI IN GENERAL POPULATION WAS 2/100 POPULATION (ONE IN FIFTY PATIENTS).**
3. **UTI WAS MORE FREQUENT IN THE OLDER AGE GROUP THAN YOUNGER IN CKD.**
4. **AMONG THE GENERAL POPULATION, UTI WAS MORE FREQUENT IN YOUNGER AGE GROUP.**
5. **FEMALES OF GENERAL POPULATION WERE MORE AFFECTED WITH UTI.**
6. **ASYMPTOMATIC UTI WAS MORE COMMON IN CKD PATIENTS.**
7. **THE COMMON PRESENTING SYMPTOMS WERE DYSURIA, URGENCY, FREQUENCY OF MICTURITION AND LOWER ABDOMINAL PAIN.**
8. **SIGNIFICANT PYURIA AND BACTERIURIA WERE MORE PREVALENT IN THE CKD PATIENTS THAN IN GENERAL POPULATION.**

9. **A HIGHER INCIDENCE OF UTI WAS FOUND AS THE SEVERITY OF CKD INCREASES.**
10. **UTI IS MORE PREVALENT IN OLIGURIC CKD PATIENTS THAN THE NONOLIGURIC PATIENTS.**
11. **GRAM NEGATIVE ORGANISMS WERE THE COMMON ISOLATES IN URINE CULTURES.**
12. **E.COLI WAS FOUND AS THE COMMONEST CAUSATIVE OF UTI IN CKD AS WELL AS IN GENERAL POPULATION.**
13. **PSEUDOMONAS WAS THE SECOND COMMONEST CAUSATIVE AGENT OF UTI IN CKD.**
14. **E.COLI WAS ALSO THE COMMONEST ORGANISM IDENTIFIED IN THE POSITIVE URINE CULTURES FOLLOWED BY KLEBSIELLA, PROTEUS AND PSEUDOMONAS.**

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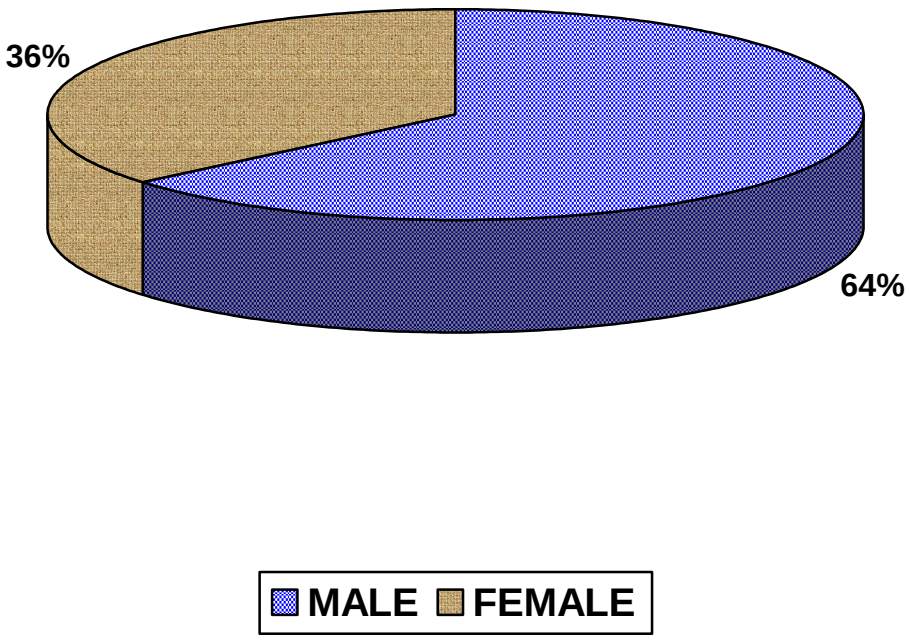
SEX DISTRIBUTION

CKD PATIENTS (GROUP A)



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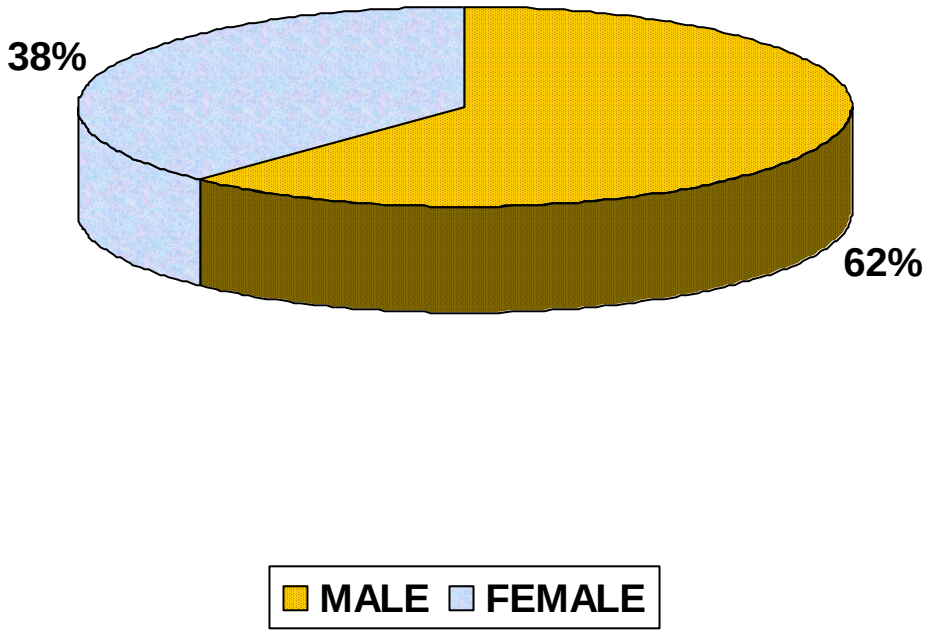
CONTROL POPULATION (GROUP B)



AGE AND SEX DISTRIBUTION

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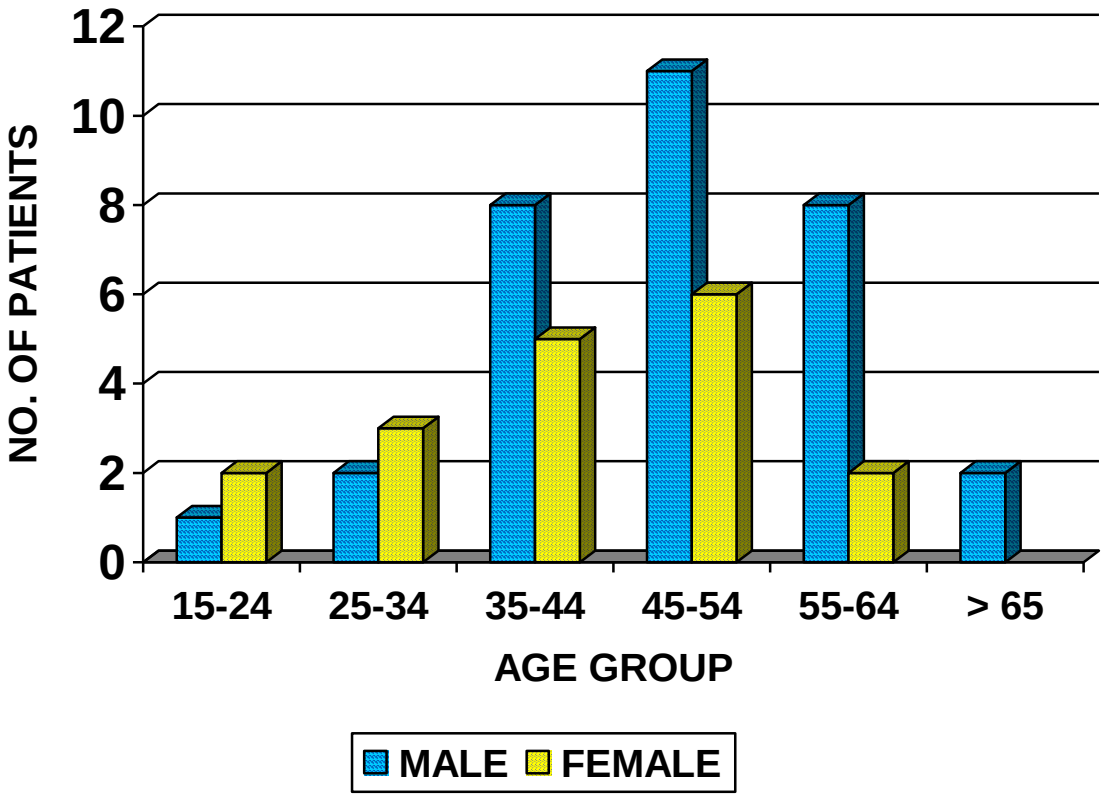
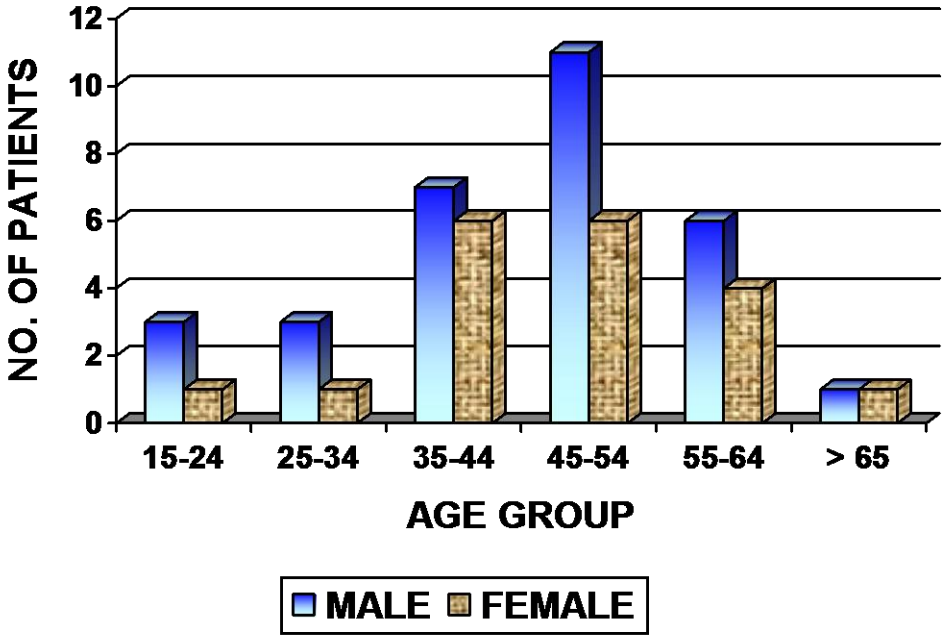
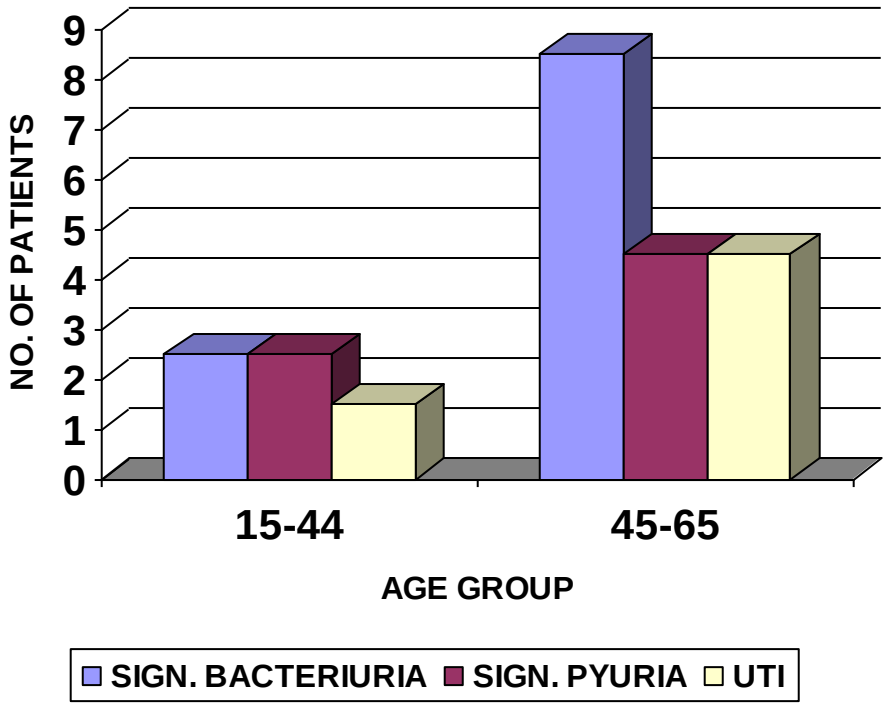


AGE AND SEX DISTRIBUTION

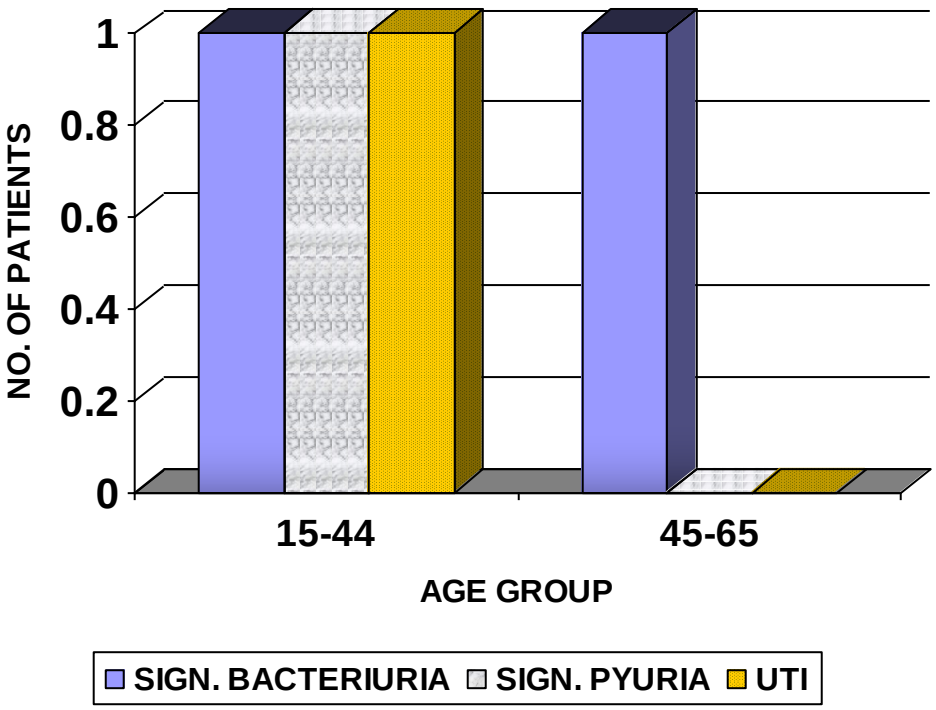
CONTROL POPULATION (GROUP B)



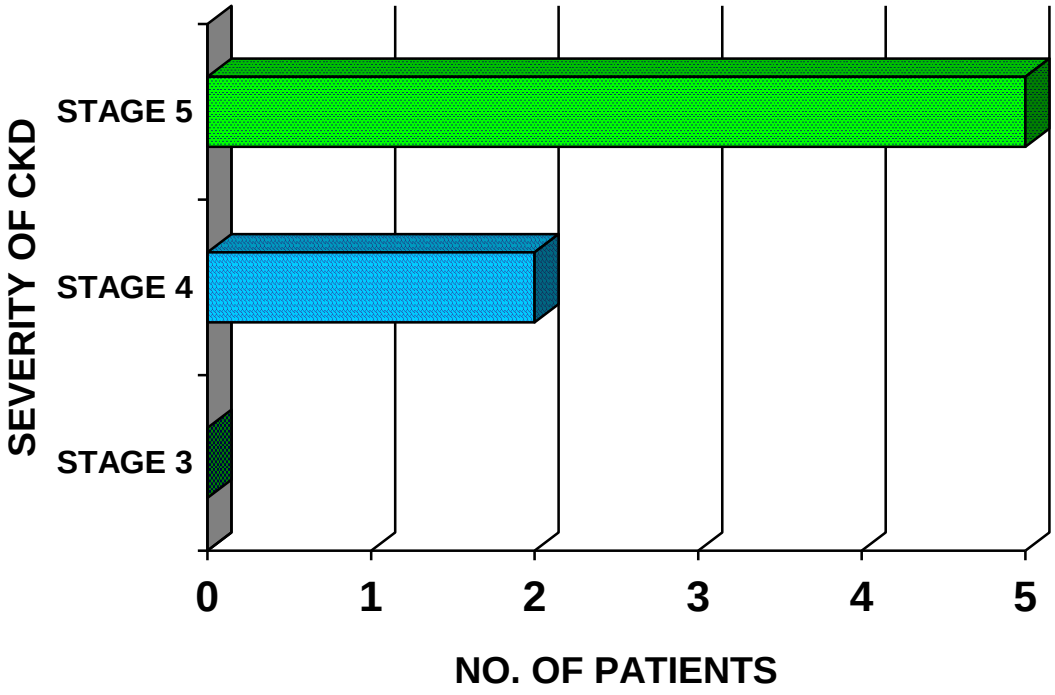
CORRELATION BETWEEN SIGNIFICANT BACTERIURIA AND SIGNIFICANT PYURIA WITH UTI, IN CKD PATIENTS



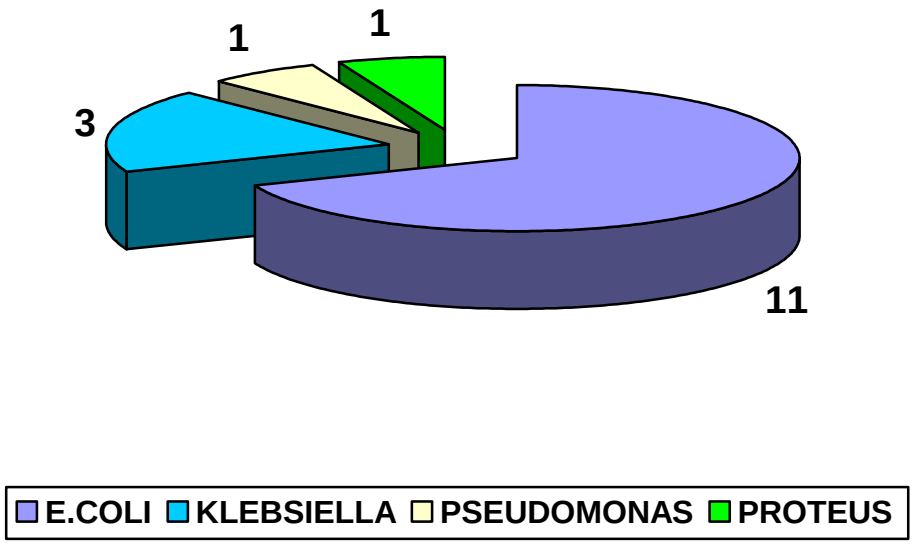
CORRELATION BETWEEN SIGNIFICANT BACTERIURIA AND SIGNIFICANT PYURIA WITH UTI, IN CONTROL GROUP


1
0.8
0.6
0.4
0.2
0
NO. OF PATIENTS
15-44
45-65
AGE GROUP
SIGN. BACTERIURIA
SIGN. PYURIA
UTI

UTI IN RELATION TO CKD IN TERMS OF SEVERITY



UROPATHOGENS IDENTIFIED IN CKD PATIENTS



PREVALENCE OF UTI IN CKD PATIENTS

PROFORMA

Name	Age	Sex	Body Weight (Kg)
OP/IP NO	Ward/op	DOA	
		DOD	

PRESENT ILLNESS:

H/O Dysuria	Yes/No
H/O Frequency	Yes/No
H/O Urgency	Yes/No
H/O Fever	Yes/No
H/O Chills / Rigor	Yes/No
H/O Flank Pain	Yes/No
H/O Abd. Distension	Yes/No
H/O Oliguria	Yes/No
H/O Recent Urinary Catheterization	Yes/No
H/O Immuno Suppressive Drugs	Yes/No

PAST HISTORY:

HT

DM

URETERIC COLIC

CKD: Duration : on PD / HD

TREATMENT HISTORY:

On antibiotics- Yes/No

Details:

EXAMINATION:

Pallor: Edema: Pulse:

BP:

CVS :

RS :

ABDOMEN :

CNS :

INVESTIGATION:

Hb%

Tc:

Dc:

Blood urea:

Sr. Creatinine:

Blood Sugar:

Sr. Sodium:

Sr. Potassium:

HIV I & II:

GFR (Cock Craft & Gault formula)

USG ABDOMEN: RK: LK: CMD: Echotexture:

Bladder:

URINE:

Albumin: Sugar: Deposit: Significant Pyuria:

CULTURE & SENSITIVITY:

Organism :

Colony count :

Significant bacteriuria :

Highly sensitive to :